SCN1A gene

sodium voltage-gated channel alpha subunit 1

Normal Function

The *SCN1A* gene belongs to a family of genes that provide instructions for making sodium channels. These channels, which transport positively charged sodium atoms (sodium ions) into cells, play a key role in a cell's ability to generate and transmit electrical signals.

The *SCN1A* gene provides instructions for making one part (the alpha subunit) of a sodium channel called NaV1.1. These channels are found in the brain and muscles, where they control the flow of sodium ions into cells. In the brain, NaV1.1 channels are involved in transmitting signals from one nerve cell (neuron) to another. Communication between neurons depends on chemicals called neurotransmitters, which are released from one neuron and taken up by neighboring neurons. The flow of sodium ions through NaV1.1 channels helps determine when neurotransmitters will be released.

Health Conditions Related to Genetic Changes

familial hemiplegic migraine

At least five mutations in the *SCN1A* gene have been identified in people with familial hemiplegic migraine type 3 (FHM3). Each of these mutations changes a single protein building block (amino acid) in the NaV1.1 channel, which alters the channel's structure. The abnormal channels stay open longer than usual, which increases the flow of sodium ions into neurons. This increase triggers the cell to release more neurotransmitters. The resulting changes in signaling between neurons make people with FHM3 more susceptible to developing these severe headaches.

malignant migrating partial seizures of infancy

other disorders

More than 150 mutations in the *SCN1A* gene have been associated with various seizure disorders that begin in infancy or childhood. Several of these conditions are relatively mild. These conditions include simple febrile (fever-associated) seizures, which start in infancy and usually stop by age 5, and generalized epilepsy with febrile seizures plus (GEFS+). GEFS+ involves febrile and other types of seizures that can persist beyond childhood. Other conditions cause more serious seizures that last longer and may be difficult to control. These recurrent seizures can worsen over time and lead to a decline in brain function. Severe seizure disorders caused by *SCN1A*

mutations include severe myoclonic epilepsy of infancy (SMEI) and intractable childhood epilepsy with generalized tonic-clonic seizures (ICE-GTC).

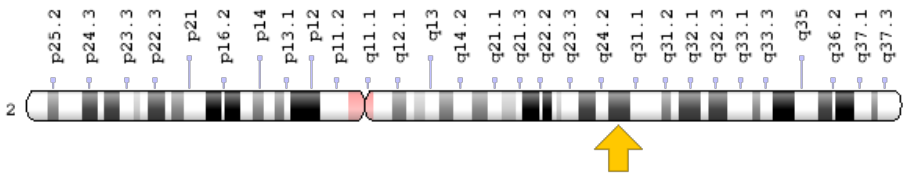
The *SCN1A* mutations that underlie seizure disorders have a variety of effects on the function of the NaV1.1 channel. The milder disorders are caused by mutations that change single amino acids in the channel, which alter the channel's structure. More severe seizure disorders can result from several different changes in the *SCN1A* gene. Some mutations lead to the production of a nonfunctional version of the NaV1.1 channel or reduce the number of these channels produced in each cell. Other mutations change single amino acids in critical regions of the channel. All of these genetic changes affect the ability of NaV1.1 channels to transport sodium ions into neurons. It is unclear, however, why these genetic changes lead to such a large range of seizure disorders.

A common change (polymorphism) in the *SCN1A* gene has been associated with the effectiveness of certain anti-seizure medications. This polymorphism, which is written as ICS5N+5G>A, alters a single DNA building block (nucleotide) in the *SCN1A* gene. Studies suggest that this polymorphism is associated with the maximum safe amount (dose) of the anti-seizure drugs phenytoin and carbamazepine. These drugs treat epilepsy by blocking sodium channels (such as NaV1.1) in neurons. A dose that is too small may not control seizures effectively, while a dose that is too large may cause unwanted side effects. Right now, doctors must use a trial-and-error approach to determine the correct dose for each person. Researchers are hopeful that doctors will one day be able to use the ICS5N+5G>A polymorphism to determine the safest and most effective dose of anti-seizure medications for each individual.

Chromosomal Location

Cytogenetic Location: 2q24.3, which is the long (q) arm of chromosome 2 at position 24.3

Molecular Location: base pairs 165,989,160 to 166,149,216 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- GEFSP2
- HBSCI
- NAC1
- Nav1.1
- SCN1
- SCN1A_HUMAN
- sodium channel protein, brain I alpha subunit
- sodium channel, voltage gated, type I alpha subunit
- sodium channel, voltage-gated, type I, alpha
- sodium channel, voltage-gated, type I, alpha polypeptide
- sodium channel, voltage-gated, type I, alpha subunit

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Specific Channels Can Rapidly Transport Ions Across Membranes
  https://www.ncbi.nlm.nih.gov/books/NBK22509/

GeneReviews

- Familial Hemiplegic Migraine
  https://www.ncbi.nlm.nih.gov/books/NBK1388
- SCN1A-Related Seizure Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1318

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SCN1A%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D

OMIM

- EPILEPTIC ENCEPHALOPATHY, EARLY INFANTILE, 6
  http://omim.org/entry/607208
- GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS, TYPE 1
  http://omim.org/entry/604233
- GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS, TYPE 2
  http://omim.org/entry/604403
- SODIUM CHANNEL, NEURONAL TYPE I, ALPHA SUBUNIT
  http://omim.org/entry/182389

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SCN1A.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SCN1A%5Bgene%5D
- HGNC Gene Family: Sodium voltage-gated channel alpha subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/1203
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10585
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6323
- UniProt
  http://www.uniprot.org/uniprot/P35498

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